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UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF CALIFORNIA

GEN-PROBE INCORPORATED,

Plaintiff,

vs.

VYSIS, INC.,

Defendant.

CASE NO. 99-CV- 2668 H (AJB)

Order Granting Motion for Partial Summary Judgment of Non-Infringement of the '338 Patent; Claim Construction of the term "Amplifying" as found in the '338 Patent

On March 13, 2001, plaintiff Gen-Probe, Incorporated filed a Second Amended Complaint for declaratory relief and unfair competition related to a patent and license agreement with the defendant Vysis, Incorporated. This case is styled as a declaratory judgment action brought by Gen-Probe. Thus, Vysis, the owner of U.S. Patent No. 5,750,338 ("the '338 patent"), is the defendant. Gen-Probe asks the Court to declare the '338 patent invalid and further declare that Gen-Probe's current and anticipated activities do not infringe any valid claims of the '338 patent. In its Second Amended Complaint, Gen-Probe asserts the following causes of action: (1) non-infringement of the '338 patent; (2) invalidity of the '338 patent; (3) declaratory relief; (4) unfair competition; (5) unenforceability of the '338 patent.

On April 30, 2001, Gen-Probe filed a motion for partial summary judgment under Counts One and Three of its Second Amended Complaint arguing that its nucleic acid test for human immunodeficiency virus ("HIV") and hepatitis C virus ("HCV") does not literally infringe the claims

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of the '338 patent held by Vysis. Specifically, Gen-Probe argues that the '338 patent describes and encompasses only methods of non-specific amplification and that its products do not incorporate non-specific amplification.

On May 25, 2001, Vysis filed its Opposition. On June 1, 2001, Gen-Probe filed its Reply. The Court held a hearing on the motion and claim construction for the term "amplifying," as found in Claims of the '338 Patent, on June 7, 2001. R. William Bowen and Stephen Swinton appeared on behalf of Gen-Probe and Charles Lipsey, John L'Estrange appeared on behalf of Vysis. Thomas Banks and Scott Orwell appeared telephonically on behalf of Vysis.

I. Scientific Background

The '338 patent relates generally to methods for use in nucleic acid diagnostics, including the use of nucleic acid "probes" to detect infectious organisms. The '338 patent describes methods by which nucleic acids may be "captured" onto solid supports and "amplified," so that small quantities of nucleic acids may be then detected by the probes.

"Target capture" techniques are used in nucleic acid methods to isolate a particular nucleic acid of interest prior to detection or other steps. In target capture methods, the target nucleic acid is bound to a solid support, such as a filter, particle, or bead, which allows the target to be removed from the sample in which it was originally contained.

In order to achieve a detectable level of target organisms in a sample, it is sometimes necessary to increase the target organism's nucleic acid through processes known as "nucleic acid amplification" by using enzymes and primers. "Polymerase" enzymes are used to copy a DNA or RNA strand and make its compliment. Primers are short pieces of DNA that are used in amplification methods to cause an enzyme, such as DNA polymerase, to start its copying at a certain point along a nucleic acid sequence. Like probes in the detection step, primers work by binding to a complementary nucleotide sequence in the target nucleic acid. Primers can either be specific or non-specific. Specific primers are designed to bind only to a pre-selected nucleic acid sequence. Non-specific or "random" primers can be used with DNA polymerase to copy random portions of the nucleic acid sequence of the target organism.

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II. The '338 Patent

The '338 patent contains six independent claims (claims 1, 7, 19, 27, 28, and 34). Each of these claims is generally directed to a method of, or kit for, capturing the target (i.e. binding a support to the target polynucleotide and substantially separating the support and bound target from the sample) and "amplifying" a target polynucleotide. Each independent claim contains the term "amplifying." For example, claim 1 provides:

> A method for amplifying a target polynucleotide contained in a sample comprising the steps of: (a) contracting the sample with a first support which binds to the target polynucleotide; (b) substantially separating the support and bound target polynucleotide from the sample; (c) amplifying the target polynucleotide.

The '338 patent specification sets forth seven examples of the methods taught by the inventors. The first three examples refer only to methods of target capture alone. Examples four through seven refer to combining target capture and methods of amplification.

III. Standard of Review

A. Motion for Summary Judgment

A motion for summary judgment shall be granted where "there is no genuine issue as to any material fact and . . . the moving party is entitled to judgment as a matter of law." Fed.R.Civ.P. 56(c); See also British Airways Bd. v. Boeing Co., 585 F.2d 946, 951 (9th Cir. 1978), cert. den., 440 U.S. 981 (1979). Determination of infringement is a two-step procedure. First, the claims are construed by the Court as a matter of law. Second, the properly construed claims are applied to the accused device, a question of fact. See Wang Laboratories, Inc. v. America Online, Inc., 197 F.3d 1377, 1380 (Fed. Cir. 1999); EMI Group North America, Inc. v. Intel Corp., 157 F.3d 887, 891 (Fed Cir. 1998).

B. Claim Construction

Claim construction is an issue of law to be decided by the Court. Markman v. Westview Instruments, Inc., 52 F.3d 967, 979 (Fed. Cir. 1995), aff'd, 517 U.S. 370 (1996). "[T]he focus in construing disputed terms in claim language is not the subjective intent of the parties to the patent contract when they used a particular term. Rather the focus is on the objective test of what one of ordinary skill in the art at the time of the invention would have understood the term to mean." Id. at 985-86.

When construing the terms of a patent, the Court must first turn to "intrinsic evidence." Intrinsic evidence includes the claim itself, the specification, and the prosecution history of the patent. Vitronics Corp. v. Conceptronic, Inc., 90 F. 3d 1576, 1582 (Fed. Cir. 1996). Established rules of claim interpretation require that the Court first consider the words of the claims themselves, "both asserted and unasserted, to define the scope of the patented invention." Id. at 1582. The words are generally given their customary and ordinary meaning. Id.; Hoechst Celanese Corp. v. BP Chemicals, Ltd., 78 F.3d 1575, 1578 (Fed. Cir. 1996) (stating that in defining technical terms, the Court should interpret it "as having the meaning it would be given by persons experienced in the field of the invention"). However, the Court must follow the definition of terms intended by the patentee if his or her special definition is clearly delineated in the specification or file history. Vitronics Corp., 90 F.3d at 1583; Hoechst Celanese Corp., 78 F.3d at 1578.

The Court also considers the specification to determine whether the inventor has employed any terms or words in a manner that is inconsistent with their plain and ordinary meaning. Vitronics, 90 F.3d at 1582. "Claims must be read in view of the specification, of which they are a part." Markman, 52 F.3d at 979. "One purpose for examining the specification is to determine if the patentee has limited the scope of the claims." Watts v. XL Sys., Inc., 232 F.3d 877, 882 (Fed. Cir. 2000).

The Court also may review the prosecution history of the patent, if admitted into evidence. Vitronics, 90 F.3d at 1582. This history is "the complete record of all the proceedings before the Patent and Trademark Office, including any express representations made by the applicant regarding the scope of the claims." Id. It also includes prior art which is cited in the file history. Id. at 1583.

The Court may resort to extrinsic evidence only if the intrinsic evidence is considered and there still remains some ambiguity as to the scope or meaning of the claim. Id. at 1583. "[I]deally there should be no 'ambiguity' in claim language to one of ordinary skill in the art that would require resort to evidence outside the specification and prosecution history." Markman, 52 F.3d at 986. Extrinsic evidence can include any evidence outside the patent and prosecution history such as prior art documents, dictionaries, technical treatises, articles, expert testimony, and inventor testimony. Vitronics, 90 F.3d at 1584. However, "extrinsic evidence in general, and expert testimony in

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particular, may be used only to help the court come to the proper understanding of the claims; it may not be used to vary or contradict the claim language." Id.

IV. Analysis

Gen-Probe argues that it is entitled to summary judgment of non-infringement because its product (the HIV/HCV Assay) uses only specific amplification. Gen-Probe asserts that the term "amplifying" as used in the '338 patent would be understood by one of ordinary skill in the art at the time of the invention to encompass only non-specific amplification. Vysis agrees that Gen-Probe's product uses specific amplification. However, Vysis contends that the '338 patent is not limited to non-specific amplification.

A. Claim Construction

In construing the term "amplifying" of the '338 patent, the Court must first turn to "intrinsic evidence." Intrinsic evidence includes the claim itself, the specification, and the prosecution history of the patent. The claim language in this case does not help determine the construction of the term "amplifying." The term "amplifying" is found in each of the principle claims without any modification.

1. Specification

Gen-Probe argues that the specification of the '338 patent supports a construction of "amplifying" to only include non-specific amplification. The Court agrees. Immediately before the Examples that teach amplification in the '338 patent, the inventors set forth their teachings with respect to amplification methods.

> The sensitivity of the above DNA or RNA target capture methods can be enhanced by amplifying the captured nucleic acids. This can be achieved by **non-specific replication** using standard enzymes...In addition, where amplification is employed following purification of the target nucleic acids as described above, the amplified nucleic acids can be detected according to other, conventional methods not employing the [techniques] described above. Amplification of the target nucleic acid sequences, because it follows purification of the target sequences can employ **non-specific enzymes or primers** (i.e. enzymes or primers which are capable of causing the replication of virtually any nucleic acid sequence). Although any background, non-target nucleic acids are replicated along with target, this is not a problem because most of the background nucleic acids have been removed in the course of the capture process. Thus **no specially tailored primers are needed** for each test, and the same standard amplification reagents can be used regardless of the targets.

'338 patent, col. 30, lines 14-40 (emphasis added).

The introduction to the amplification techniques only addresses the possibility of using non-specific amplification methods. Vysis argues that the language permissive such that while "non-specific" methods "can be" used, they need not be. Vysis concedes that it did not invent specific or non-specific amplification. Rather, Vysis argues that its contribution to the science was the idea of target capture plus amplification. Vysis states that the patent focuses on the combination of the two, not describing amplification methods. Without target capture prior to amplification, non-specific amplification would not be a viable technique for detecting target nucleic acids in a sample. Vysis argues that the specification tells those of ordinary skill in the art that, while the use of target capture made it possible to use non-specific amplification in assays for detecting nucleic acids, the invention was more generally directed to the use of target capture prior to either specific or non-specific amplification. However, if the inventors wanted to teach that either method could be used they could have included at least one sentence or reference to specific amplification. They did not.

Vysis contends that a parenthetical sentence in Example 5 of the Specification does explicitly set forth the idea of specific amplification. The Specification of the '338 patent includes four Examples which teach the amplification techniques disclosed in the patent. Vysis agrees that Examples 4, 6 and 7 only teach non-specific amplification.[1] The parties dispute the proper interpretation of the description set forth in Example 5 of the Specification. Example 5 provides:

> In this example, both non-specific replication of target DNA and transcription of that DNA are used to amplify capture DNA. Referring to FIG. 5, ...Because the primers are random, some will, simple as a matter of statistics, bind to and cause replication of sample sequences, no matter what those sequences are. (Alternatively, the double stranded DNA can be formed by synthesis starting from capture probe a.)

'339 patent, col. 31, lines 24-26, 44-48.

Vysis contends that the parenthetical disclosure indicates that the capture probe is used as a specific primer to the target DNA and thus discloses "specific amplification." However, the explicit language of Example 5 (i.e. "non-specific replication" and "random" primers) refers only to non-specific amplification. In addition, Example 5 incorporates Figure 5, of the drawings in the patent.

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[1] For example, Example 4 describes a method of non-specific amplification using polymerases that lack transcriptional specificity ('338 Patent, col. 30, lines 59-68) and Example 6 describes amplification using random hexamer primers to "bring about non-specific double-stranded DNA synthesis." ('338 patent, col. 31, lines 57-64).

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In discussing Figure 5, the inventors state, "In Step 3 of FIGS. 4, 5 and 6, the isolated target is non-specifically amplified to form a multitude of amplification products."

The words "specific amplification" or "PCR" do not appear in the Specification of the '338 patent. Vysis contends this is because the term "amplifying" was always used and meant to be used in its broadest sense, which includes both specific and non-specific amplification. However, the Federal Circuit has made clear that although the specification of a patent need not present every embodiment of the invention and the claims are not limited to the preferred embodiment of the invention, the claims can not enlarge what is patented beyond what the inventor has described as the invention. See Wang Laboratories, Inc. v. America Online, Inc., 197 F.3d 1377, 1383 (Fed. Cir. 1999); SciMed Systems, Inc. v. Advanced Cardiovascular Systems, Inc., 242 F.3d 1337, 1341 (Fed. Cir. 2001).

In Wang Labs, the Federal Circuit determined that although the term "frame" had meaning in general usage that encompassed both bit-mapped and character-based protocols, the specification only described and taught character-based display frames. Thus, the Court limited the claims to the only teaching set forth in the embodiment. In reaching its conclusion, the Court held that claims should not be interpreted to have a meaning or scope that would lead to their invalidity. Wang Labs, 197 F.3d at 1382-83. The Court held that the requirements of 35 U.S.C. § 112 (written description and enablement) could not be met with respect to protocols other than character-based frames. Id.

In this case, a motion for invalidity pursuant to 35 U.S.C. § 112 is not before the Court. However, the specification of the '338 patent does not describe specific amplification methods and does not teach any benefits from the combination of target capture and specific amplification. In fact, the specification teaches that you do not need to do specific amplification. The specification refers to specially tailored primers only to state that they are not necessary when an initial target capture step is used. In addition, Example 5 teaches non-specific replication of target DNA using random primers and non-specific transcription. The parenthetical reference to an "alternative" method, does not teach that such a method constitutes specific amplification or that the capture probe functions as a specific primer. The plain reading of Example 5 and Figure 5 is that they teach non-specific amplification. The Court will try to construe claims, when feasible, to sustain their validity. The Court finds it

difficult to construe "amplifying" to include specific amplification based on the disclosures in the specification that would satisfy the written description requirement of 35 U.S.C. § 112.

Recently the Federal Circuit in SciMed Systems stated, "[w]here the specification makes clear that the invention does not include a particular feature, that feature is deemed to be outside the reach of the claims of the patent, even though the language of the claims, read without reference to the specification, might be considered broad enough to encompass the feature in question." SciMed, 242 F.3d at 1341. The Court concludes that the specification supports Gen-Probe's contention that the term "amplifying" as used in the '338 patent only encompasses non-specific amplification.

2. Prosecution History

Vysis contends that the prosecution history makes clear that both the patent owner and the PTO considered the claimed invention to include PCR, a type of specific amplification. The original claims of the '338 patent were rejected by the PTO, citing the PCR patents. Vysis argues that this must mean that the PTO understood the '338 patent to include specific amplification techniques. Vysis also points to a response by the patent owner to the PTO, indicating that "[t]argets can be amplified by a number of ways including PCR." Banks Decl., Ex. E, p. 18. Finally, in the Examiner's Statement of Reasons for Allowance the Patent Examiner states, "[t]he claims are drawn to methods of PCR amplification wherein the target is first separated from the sample by using a support that binds to the target polynucleotide and then amplified." Banks Decl., Ex. F, p. 2.

Vysis argues that the Patent Examiner's understanding of the meaning of patent claims developed during prosecution is relevant to construing the proper scope and meaning of those terms. See Markman, 52 F.3d. At 983.

Gen-Probe asserts that the rejection by the PTO of the patent application based on the Mullis (PCR) patent does not support the claim that the patent covered PCR amplification methods. Vysis acknowledged in oral argument that did not have a license to the Mullis patents or PCR method. Gen-Probe argues that the patent application was rejected as obvious in light of the PCR patents because specific capture methods plus non-specific amplification were an attempt to achieve the same results as PCR. Gen-Probe also contends that statements made by the patent owner to the Patent Examiner in 1995, eight years after the application was first filed, were made too late to determine how a person

skilled in the art would have understood the invention as of the date of filing.

The focus of claim construction is how a person skilled in the art would have understood the claimed invention in the patent at the time of filing. Markman, 52 F.3d at 985-986. The prosecution history indicates that the patent application was rejected at least three times by the PTO for being obvious in light of a combination of target capture and amplification patents, including the Mullis (PCR) patents. However, despite the fact that the patent owner was clearly aware PCR, it failed to explicitly include specific amplification methods in the teachings of the patent. The prosecution history does not help explain this omission.

The Court concludes that the references to the Mullis patents and PCR in the prosecution history do not help clarify the proper construction of the term "amplifying" as used in the '338 patent. At most, the prosecution history indicates that the idea of amplification by first using specific target capture techniques is close enough to the goals of PCR to be "obvious" to the PTO in light of the Mullis patents.[2]

3. Extrinsic Evidence

Gen-Probe argues that the inventor's own testimony about the scope and intent of the patent confirms that "amplifying" includes only non-specific amplification. The Court only uses extrinsic evidence to help it come to the proper understanding of the claim terms. The Court will not use extrinsic evidence to vary or contradict claim terms. See Vitronics, 90 F.3d at 1584.

Gen-Probe has submitted testimonial and documentary evidence from the inventors of the '338 patent. Gen-Probe highlights the testimony of inventor Jon Lawrie. Lawrie stated that the '338 patent, "was directed to methods separate from PCR." Lawrie Depo. at 178:19-180:11. Similarly, inventor Walter King testified that specific amplification was not discussed at the meeting of the inventors in 1986 because the objective was to find an alternative to PCR. King Depo. at 184-186. King stated, "I think that at the highest level we were looking for amplification methods that did not involve PCR amplification." King Depo. at 45:10-15. King also testified that he did not understand the inventors

[2] In addition, an early drawing by inventor Jon Lawrie indicates that he was concerned that the use of "specific capture and non-specific amplification" was "too close" to the PCR method invented by Mullis and others at Cetus Corp. (Exh. 12).

to be claiming as their invention a combination of target capture and specific amplification. King Depo. at 136:14-21.

Gen-Probe also points to a letter written by Dr. James Richards, Director of Business Development and Licensing for Gene-Trak Systems, to one of Gene-Trak's partners stating:

> Cetus, Sibia/Salk, Biotechnica, etc. all claim specific primers for amplification whereas the present invention claims uses of the opposite, namely non-specific primer or promoters...Following extensive washing, captured target polynucleotides could be released and the non-specific amplification process could take place.

Jaczko Decl., Ex. 1, pg. 2.

Vysis argues that the testimony former employees of Vysis' predecessor company Gene-Trak Systems should be given no weight because there can be "significant difference between what an inventor thinks his patented invention is and what the ultimate scope of the claims is after allowance by the PTO." Markman, 52 F.3d at 985. However, Vysis' argument is more appropriately raised when inventor try to expand the scope of the patent claims by testifying about their subjective intent, over the description set forth in the specification. In this case, the specification supports a construction of the term "amplifying" to include only non-specific amplification and the inventors' testimony supports this construction.

While the Court does not use extrinsic evidence to construe claim terms, the evidence offered by Gen-Probe helps explain the context of the '338 patent. In particular, the inventor's testimony and the Richards' letter explain why there is no explicit reference in the specification to amplification using PCR. The extrinsic evidence in this case supports the conclusion that one of ordinary skill in the art at the time of the invention would have understood the term "amplifying" to mean non-specific amplification.

Based on the explicit language of the specification, the repeated reference to non-specific amplification methods, and the absence of any reference to specific amplification or PCR, the Court construes the term "amplifying" as found in the claims of the '338 patent to encompass only non-specific amplification. The Court finds that one of ordinary skill in the art as of December 1987 would have understood from the specification that the inventors' method combined target capture and non-specific amplification. This conclusion is reinforced by the inventors' testimony and the Richards' letter.

B. Infringement

After construing the term "amplifying" the Court can turn to question of literal infringement. Literal infringement requires that the accused device contain each limitation of the claim. Bayer AG v. Elan Pharm. Research Corp., 212 F.3d 1241, 1247 (Fed. Cir. 2000). In this case, Gen-Probe's Assay uses a target-specific amplification technology. Vysis admits that Gen-Probe's product uses specific amplification. There is no issue of material fact which would prevent the Court from ruling on infringement in a motion for summary judgment. Since the Court has construed the term "amplifying" to encompass only non-specific amplification, the Court concludes that Gen-Probe does not literally infringe the claims of the '338 patent.

V. Conclusion

For the reasons set forth above, the Court GRANTS Gen-Probe's Motion for Partial Summary Judgement of non-infringement of the claims of the '338 patent.

IT IS SO ORDERED.

DATED: 6/19/01

Marilyn L. Huff
MARILYN L. HUFF, Chief Judge
UNITED STATES DISTRICT COURT

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